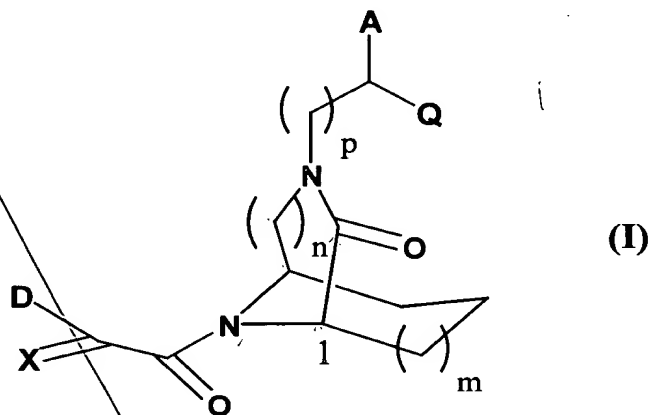


CLAIMS

What is claimed is:

1. A compound having the formula (I)



and pharmaceutically acceptable salts thereof, wherein:

X is O or F₂;

n is 1 or 2;

m is 0, 1, or 2;

p is 0 or 1;

wherein the stereochemistry at carbon position 1 is R or S;

D is (C₁-C₆)-straight or branched alkyl, (C₂-C₆)-straight or branched alkenyl,

(C₅-C₇)-cycloalkyl or (C₅-C₇)-cycloalkenyl substituted with (C₁-C₄)-straight or branched alkyl or (C₂-C₄)-straight or branched alkenyl, O-(C₁-C₄)-straight or branched alkyl, O-(C₂-C₄)-straight or branched alkenyl, 2-indolyl, 3-indolyl, [(C₁-C₄)-alkyl or (C₂-C₄)-alkenyl]-Ar or Ar;

Ar is a carbocyclic aromatic group selected from the group consisting of phenyl, 1-naphthyl, 2-naphthyl, indenyl, azulenyl, fluorenyl, and anthracenyl; or a heterocyclic aromatic group selected from the group consisting of 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, 1,2,3-oxadiazolyl, 1,2,3-triazolyl, 1,3,4-thiadiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, 1,3,5-triazinyl, 1,3,5-trithianyl, indolizinyl, indolyl, isoindolyl, 3H-indolyl, indolinyl, benzo[b]furanyl, benzo[b]thiophenyl, 1H-indazolyl, benzimidazolyl, benzthiazolyl, purinyl, 4H-quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, 1,8-naphthyridinyl, pteridinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, and phenoxazinyl;

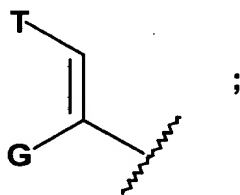
Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halogen, hydroxyl, hydroxymethyl, nitro, trifluoromethyl, trifluoromethoxy, (C₁-C₆)-straight or branched alkyl, (C₂-C₆)-straight or branched alkenyl, O-[(C₁-C₄)-straight or branched alkyl], O-benzyl, O-phenyl, 1,2-methylenedioxy, amino, carboxyl, N-[(C₁-C₅)-straight or branched alkyl or (C₂-C₅)-straight or branched alkenyl] carboxamides, N,N-di-[(C₁-C₅)-straight or branched alkyl or (C₂-C₅)-straight or branched alkenyl] carboxamides, N-morpholinecarboxamide, N-benzylcarboxamide, N-thiomorpholinocarboxamide, N-picolinoylcarboxamide, O-W, CH₂-(CH₂)_q-W, O-(CH₂)_q-W, (CH₂)_q-O-W, and CH=CH-W;

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W is 4-methoxyphenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrazyl, quinolyl, 3,5-dimethylisoxazolyl, isoxazolyl, 2-methylthiazoyl, thiazoyl, 2-thienyl, 3-thienyl, or pyrimidyl; q is 0-2;

Q and A are independently hydrogen, Ar, (C₁-C₁₀)-straight or branched alkyl, (C₂-C₁₀)-straight or branched alkenyl or alkynyl, (C₅-C₇)-cycloalkyl substituted (C₁-C₆)-straight or branched alkyl, (C₂-C₆)-straight or branched alkenyl or alkynyl, (C₅-C₇)-cycloalkenyl substituted (C₁-C₆)-straight or branched alkyl, (C₂-C₆)-straight or branched alkenyl or alkynyl, or Ar-substituted (C₁-C₆)-straight or branched alkyl, (C₂-C₆)-straight or branched alkenyl or alkynyl wherein, in each case, any one of the CH₂ groups of said alkyl, alkenyl or alkynyl chains may be optionally replaced by a heteroatom selected from the group consisting of O, S, SO, SO₂, N, and NR, wherein R is selected from the group consisting of hydrogen, (C₁-C₄)-straight or branched alkyl, (C₂-C₄)-straight or branched alkenyl or alkynyl, and (C₁-C₄)-bridging alkyl wherein a bridge is formed between the nitrogen and a carbon atom of said heteroatom-containing chain to form a ring, and wherein said ring is optionally fused to an Ar group; or



G is hydrogen, (C₁-C₆)-straight or branched alkyl or (C₂-C₆)-straight or branched alkenyl or alkynyl; and

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cont

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T is Ar or substituted 5-7 membered cycloalkyl with substituents at positions 3 and 4 which are independently selected from the group consisting of oxo, hydrogen, hydroxyl, O-(C₁-C₄)-alkyl, or O-(C₂-C₄)-alkenyl.

2. A compound of claim 1 wherein:

the stereochemistry at carbon 1 is S;

m is 0 or 1;

n is 1;

p is 1;

X is O or F₂;

D is 3, 4, 5-trimethoxyphenyl or t-pentyl;

Q and A are independently hydrogen; 2, 3, or 4-pyridyl; or phenyl-substituted (C₁-C₆)-straight or branched chain alkyl, wherein phenyl is optionally substituted with one to three substituents independently selected from (C₁-C₆) alkyl, O-(C₁-C₆) alkyl, carboxyl and trifluoromethyl, wherein said alkyl is straight or branched.

3. A compound of claim 1 wherein:

the stereochemistry at carbon 1 is S;

X is O;

m is 1;

n is 1;

p is 1;

A is 3-phenylpropyl, 2-phenylethyl, 2-(3,4-dimethoxyphenyl)ethyl, 3-(3,4,5-trimethoxyphenyl)propyl or 3-(3,4-dimethoxyphenyl)propyl; and

Q is 3-phenylpropyl, 2-phenylethyl, 3-(3,4,5-trimethoxyphenyl)propyl, 2-(3,4-dimethoxyphenyl)ethyl or 3-(3,4-dimethoxyphenyl)propyl.

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4. A compound of claim 1 wherein:

the stereochemistry at carbon 1 is S;

X is O;

m is 1;

n is 1;

p is 0;

A is hydrogen; and

Q is 2-(3,4,5-trimethoxyphenyl)ethyl, 2-(3,4-dimethoxyphenyl)ethyl, 3-(3,4-dimethoxyphenyl)propyl, 2-phenylethyl, 3-phenylpropyl, 4-phenylbutyl or 2-(3-pyridyloxy)ethyl.

5. A compound of claim 1 wherein:

the stereochemistry at carbon 1 is S;

X is O;

m is 1;

n is 0;

p is 1;

A is 3-phenylpropyl, 2-phenylethyl, 2-(3,4-dimethoxyphenyl)ethyl, 3-(3,4,5-trimethoxyphenyl)propyl or 3-(3,4-dimethoxyphenyl)propyl; and

Q is 3-phenylpropyl, 2-phenylethyl, 3-(3,4,5-trimethoxyphenyl)propyl, 2-(3,4-dimethoxyphenyl)ethyl or 3-(3,4-dimethoxyphenyl)propyl.

6. A compound of claim 1 wherein:

the stereochemistry at carbon 1 is S;

X is O;

m is 1;

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n is 0;

p is 0;

A is hydrogen; and

Q is 2-(3,4,5-trimethoxyphenyl)ethyl, 2-(3,4-dimethoxyphenyl)ethyl, 3-(3,4-dimethoxyphenyl)propyl, 2-phenylethyl, 3-phenylpropyl, 4-phenylbutyl or 2-(3-pyridyloxy)ethyl.

7. A pharmaceutical composition which comprises as an active ingredient an amount of a compound as claimed in any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, effective for stimulating neurite growth in nerve cells, and one or more pharmaceutically acceptable carriers, excipients or diluents thereof.

8. A method for stimulating neurite growth in nerve cells comprising the step of contacting said nerve cells with a composition comprising a neurotrophic amount of a compound with affinity for an FK506 binding protein as claimed in any one of claims 1-6.

9. A method for stimulating neurite growth in nerve cells comprising the step of contacting said nerve cells with a composition comprising a neurotrophic amount of a compound with affinity for FKBP12 as claimed in any one of claims 1-6.

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